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+351 289 800066; E-mail: maalves@ualg.pt**Keywords:** Decavanadate; Anticancer; Polyoxometalates (Poms)<https://www.peertechz.com>

Short Communication

The Role of Decavanadate in Anti-Tumour Activity

Abstract

Decavanadate compounds were described to be involved in a variety of biological activities and responses such as anti-virus, anti-bacterial and anticancer. While the mechanisms of action of the anti-viral and anti-bacterial activities are better understood, the same does not go for the anti-tumour activity. Nevertheless, the inhibition of tumour proliferation seems to impact certain enzymes such as alkaline phosphatase, ecto-nucleotidases or P-type ATPases. In the present report, several studies are described, in a way to explain the increasing interest of these polyoxometalate in cancer therapy. The detailed knowledge of the molecular basis of decavanadate–proteins and cellular interactions allows to better understand the processes associated with the anticancer applications, not only for decavanadate but as well for other polyoxometalates (POMs).

Introduction

Cancer incidence is growing every year all around the world, as well as the resistance of already used metal drugs like cis-platin. Indeed, in 2012 the global burden of cancer rose to 14,1 million of new cases and 8,2 millions of death per cancer comparing with 12,7 million and 7,6 million respectively in 2008. The most frequent diagnosed cancers in the world are the pulmonary one (1,8 million cases, i.e. 13,0% of the total), the breast one (1,7 million, i.e. 11,9%) and the colorectal one (1,4 million cases, i.e. 9,7%). Due to the global aging and the population growth, it was estimated that in 2025 there will be a substantial increase of new case of cancer per year of 19,3%. Besides the effectiveness and resistance effect, chemotherapeutic agents, as cisplatin or gemcitabine, are also known for their high toxicity. Taking this into account, polyoxometalates have been selected by some researchers as alternative anti-tumour substances with promising results in tumour growth suppression [1–11].

Polyoxometalates are interesting compounds possessing a rich diversity of structure and size with large redox chemistry and a high solubility in aqueous solutions. Thanks to these properties and others, POMs are studied and used in a large scale of fields, and have become of a great interest in medicine. Indeed many polyoxometalates have proved to be efficient against virus, bacteria and tumour cells. Polyoxometalates (POMs) are inorganic oligomeric assemblies of transition-metal (such as vanadium, molybdenum, tungsten) and oxygen atoms. Examples of POM's structure includes Lindqvist (isopoly

compound), Anderson (hetero atoms on the surface), Keggin (hetero atom in the core), Wells–Dawson (2 hetero atoms) and Preyssler (various kind of hetero atoms). The Lindqvist type of POMs, such as decavanadate (V_{10}) (Figure 1), as well as the Dawson type are known for their biological activities against virus, bacteria and more recently against tumour cells but recently others POMs types are of increasing interest in several areas of research [1–11].

Decavanadate anti-cancer activities

Vanadium is a trace element widely distributed in plants and animals although its essential role for humans is yet to be clarified. Vanadium impact in biology, pharmacology and medicine is well known, mainly after the discovery that the “muscle inhibitor factor”, present in ATP obtained from horse

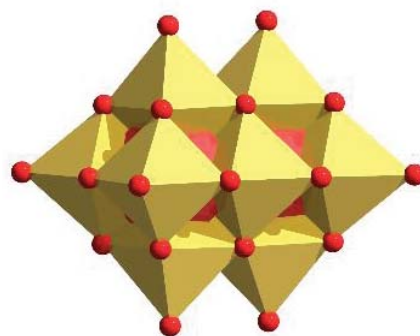


Figure 1: Structural representation of decavanadate species. V10O286-. The red spheres represent oxygen atoms.

muscle and responsible for Na^+ , K^+ -ATPase inhibition was, in fact, vanadate [12]. Vanadate is also known as a potent inhibitor of protein tyrosine phosphatases, described as one the main targets of vanadate as an insulin enhancement agent, promoting an increasing of glucose uptake in several types of cells, among others effects that prevent diabetes [13].

Decavanadate, an oligomer with 10 octahedral vanadium(V) centres ($\text{V}_{10}\text{O}_{28}^{6-}$), exerts numerous physiological roles, not only *in vitro*, but also *in vivo*, and is known to interact with a wide range of biomolecules [14,15]. Besides the insulin mimetic behavior, decavanadate and decavanadate compounds were described to be involved in a variety of biological activities and responses such as anticancer, anti-bacterial and anti-virus [16–20]. In the last years, several papers have been published regarding the anti-tumour activity of decavanadate [8,19,20].

The most cited paper regarding to decavanadate (V_{10}) in biology is the interaction of V_{10} in a spatially selective manner within the protein cages of virions [18]. It seems that polyoxometalates (POMs) such as decavanadate are able to inhibit the virus activities by preventing the virus-cell host binding [18]. However, the anti-tumour activity of decavanadate is less understood and more recent than the anti-viral one. In 2010, Li et al., synthesized two decavanadates compounds and tested their anti-tumour activity *in vitro* against human lung carcinoma cells (A549) and murine leukaemia cells (P388) [8]. Both compounds exhibited lower inhibition than cis-platin compounds, whereas the decavanadate compound with a higher lipophilic effect, thus enhancing its penetration through the lipid bilayer of the cell membrane, showed higher inhibitory activity [8]. Others decavanadate complexes were showing apoptotic mechanism of cell death and also lower activities than platin compounds [8,19,20].

Abnormal levels of alkaline phosphatase (ALP) in the serum are detected in cancer patients since tumours are abnormal cellular growth proliferating faster than a normal cell [21]. Inhibition of ALP will affect tumour cell metabolism and function. Decavanadate species were recently described as stronger inhibitors of phosphatases such as ALP. Decavanadate and others POMs were assessed for their inhibitory effect on ALP and as putative anti-tumour agent [22], and results demonstrated more than 70% inhibition on intestinal alkaline phosphatase. Therefore, decavanadate demonstrated inhibition on several alkaline phosphatases, suggesting that decavanadate similarly to others POMs, inhibit abnormal cellular growth.

Decavanadate and POMs in the future of cancer therapy

As cancer incidence is growing every year all around the world it has become crucial to find drugs with low toxicity and high efficiency on normal and tumour cells, respectively. Polyoxometalates such as decavanadate are interesting compounds possessing a rich and diversity biochemistry that have become of a great interest in medicine in the last years. Indeed many polyoxometalates have proved to be efficient against virus, bacteria and tumour cells. Although the mechanism of action of decavanadate complexes and

species as anti-tumour agent is not yet fully understood, the decavanadate effects on tumor proliferation might, at least in part, be due to the inhibition of certain enzymes such as alkaline phosphatases, ecto-nucleotidases as well as P-type ATPases. The detailed knowledge of the molecular basis of decavanadate-proteins and cellular interactions will allowed to better understand the processes associated with the anticancer applications of decavanadate as well as for others POMs.

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